

“Shim pulses” for NMR spectroscopy in inhomogeneous magnetic fields

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NMR spectroscopy conveys information about chemical structure through ppm-scale shifts of the resonance frequency depending on the chemical environment. In order to observe these small shifts, magnets with highly homogeneous magnetic field B_0 are used. The high cost and large size of these magnets are a consequence of the requirement for high homogeneity. In this contribution we introduce a new method for recording high-resolution NMR spectra from samples in inhomogeneous B_0 , opening up the possibility of exploiting magnets of lower homogeneity and cost. Instead of using the traditional B_0 “shim coils”, adiabatic radiofrequency (RF) pulse sequences and modulated B_0 gradients generated by coils in the probe are used to produce “shim pulses”.

A great deal of work has been devoted to finding methods for retrieving chemical shift information even when B_0 is inhomogeneous. One class of methods relies on zero- or multiple quantum coherences which evolve independently of B_0 .^{1–5} These methods are inherently two-dimensional and the high-resolution information is obtained indirectly. In order to minimize experimental time it is desirable to acquire a high-resolution spectrum directly just as for traditional NMR in homogeneous fields. A further advantage with direct acquisition is that modification of already existing multidimensional NMR techniques is facilitated. A fundamentally different approach utilizes inhomogeneity of the RF magnetic field to periodically refocus the phase dispersion from the inhomogeneous B_0 .^{6–9} With this technique a high-resolution spectrum can indeed be acquired in a single shot. The main drawback is the requirement for spatial matching between the RF and B_0 inhomogeneities. Based on this latter technique we propose the use of “shim pulses”, *i.e.* modulated, spatially constant, B_0 gradient pulses together with spatially homogeneous adiabatic frequency sweeps to induce non-linear phase shifts in three dimensions. An intuitive understanding of the approach can be obtained from the following: An adiabatic full passage applied to transverse magnetization effectively rotates the magnetization in the transverse plane with an amount that depends on the frequency offset. In homogeneous B_0 this gives rise to a “phase roll” across the NMR spectrum.¹⁰ If the adiabatic full passage is

applied in the presence of a constant B_0 gradient, a phase shift approximately linear in space will be the result. A second adiabatic passage reverses this phase shift and the adiabatic double passage constitutes effectively a 360° pulse. However, if the amplitude of the B_0 gradient is changing during the adiabatic passages, phase shifts, which are non-linear in space, can be achieved. With a proper choice of the RF and gradient modulation functions, the phase dispersion from the inhomogeneous B_0 can be cancelled. Application of a shim pulse between each detected point in the time-domain NMR signal yields an NMR spectrum free from the broadening caused by the B_0 inhomogeneity.

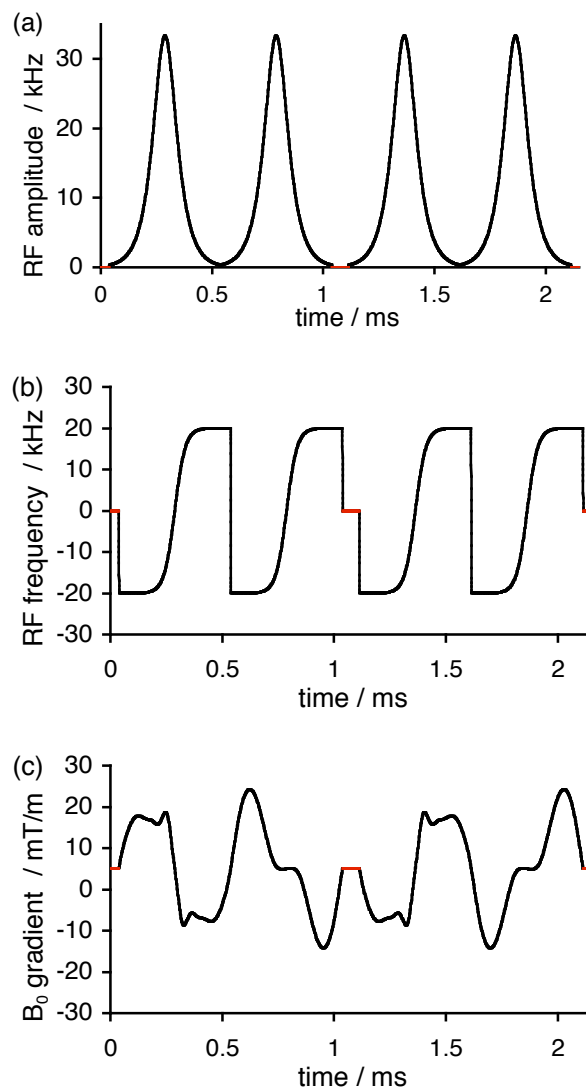


Figure 1. “Shim pulse” designed for simultaneous linear and quadratic corrections of the main magnetic field using spatially homogeneous RF pulses with amplitude (a) and frequency (b) modulation of the sech/tanh type, in conjunction with an amplitude modulated B_0 gradient (c). The total gradient waveform is a superposition of a constant baseline yielding the linear correction, and a smoothly modulated waveform, being numerically optimized to give a quadratic correction independent of chemical shift and without giving rise to non-adiabatic transitions. Effective chemical shift evolution takes place in the time intervals indicated with red color.

B_0 gradients in three orthogonal directions and spatially homogeneous RF are sufficient to induce non-linear phase shifts in three dimensions, the magnitude and degree of non-linearity of the phase shift being limited by the maximum available RF power and gradient strength, and the rate with which these can be modulated. The proposed scheme can be implemented with commercial probes developed for magnetic resonance imaging or high-resolution solution state NMR. The phase shift as a function of space depends in a complicated, strongly non-linear, way on the details of the gradient amplitude modulation and the adiabatic frequency sweeps. This non-linearity makes a general analytical description of the phenomenon difficult to accomplish. However, the non-linearity is also the strength of the method since a wide range of shapes of the phase shift can be realized by modification of the RF- and gradient waveforms using only one RF- and three gradient coils in contrast to the traditional bulky shim stack consisting of a large number of independent coils. Chemical shift artifacts can be avoided by either use of strong enough gradients to make the offset frequency as a function of position much larger than offset as a function of chemical shift. Alternatively, the gradient modulation can obey some simple symmetry rules. A smooth gradient modulation is preferred in order to avoid non-adiabatic transitions.

An experimental demonstration of the method was carried out on a Bruker Avance-700 spectrometer, operating at 700 MHz for ^1H , using a Bruker triple-resonance probe with x -, y -, and z -gradient coils. The sample was 5 mg/ml thiamine hydrochloride (vitamin B_1) in D_2O in a standard 5 mm sample tube. Accumulating 64 transients using a recycle delay, which was short in comparison to the relaxation time of water, suppressed the signal from the residual HDO. A limited amount of sample (~ 1.5 cm sample height) was used in order to assure RF homogeneity at the expense of slightly deteriorated line shapes. The main magnetic field was made inhomogeneous by (mis)adjusting the z^1 and z^2 shim coils. A smooth z -gradient modulation was numerically optimized to give rise to a quadratic phase shift along the z -axis across the sample volume. When this modulated gradient waveform is added to a constant gradient, simultaneous linear and quadratic corrections are possible. The resulting shim pulse is shown in Figure 1. Each shim pulse consists of four identical sech/\tanh^{11} adiabatic passages sweeping a frequency range of 40 kHz with a peak RF amplitude of 33 kHz. The time domain NMR signal was recorded during a train of 1024 interleaved shim pulses and free precession delays. For each 2 ms shim pulse, 150 μs of chemical shift evolution took place. The experimental NMR spectra are shown in Figure 2. The spectrum obtained with inhomogeneous B_0 without applied z -gradients has a poor signal-to-noise ratio and lacks the fine details. A constant gradient corrects for the z^1 term of the inhomogeneity yielding a spectrum with highly asymmetric peaks, which are typical for a z^2 inhomogeneity. With full gradient modulation the homogeneous spectrum is recovered.

In conclusion, we have demonstrated a novel way of obtaining high-resolution NMR spectra from samples in inhomogeneous B_0 . The spectra can be acquired in a single shot without the need for spatial matching between the inhomogeneous RF and B_0 fields. With coils producing B_0 gradients in three orthogonal directions, non-linear corrections in three dimensions are possible. The method relies on relatively simple hardware but sophisticated modulation of RF amplitude, RF frequency (or phase), and gradient amplitude. Based on contemporary development of digital generation of

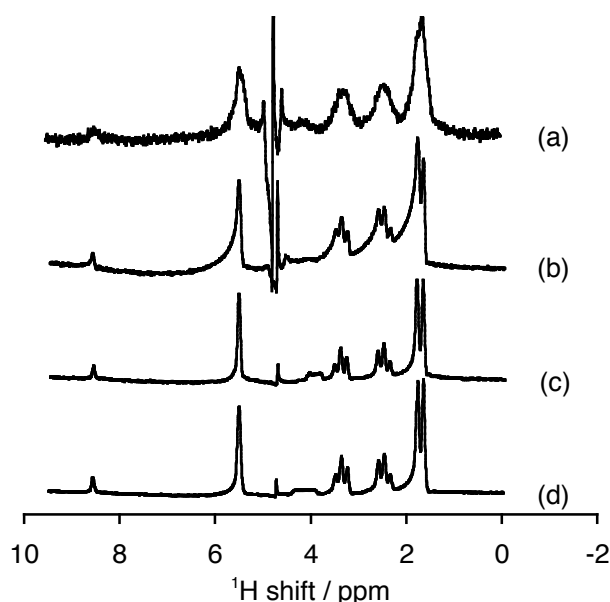
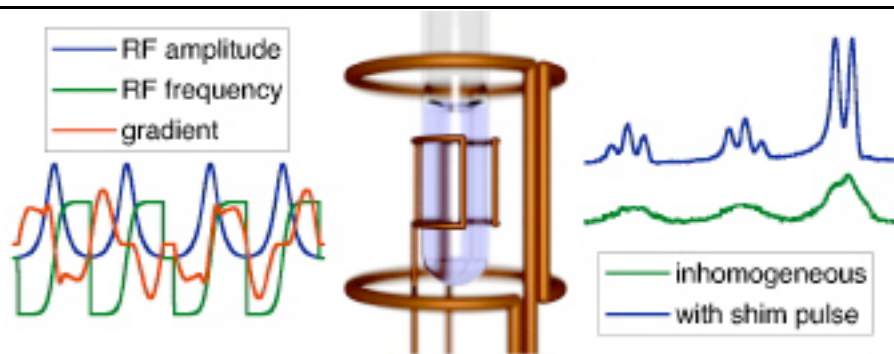


Figure 2. ^1H NMR spectra for vitamin B_1 in D_2O . (a) inhomogeneous magnetic field, (b) inhomogeneous magnetic field with linear correction, (c) inhomogeneous magnetic field with linear and quadratic correction, (d) homogeneous magnetic field. The experimental artifacts between 4 and 5 ppm originate from partially suppressed HDO and non-adiabatic transitions. The spectra are scaled to equal maximum intensity of the peak at 5.5 ppm. On an absolute intensity scale the peak amplitudes in (a) are a factor of 3 smaller than in (c), while the intensities in (c) and (d) are comparable.

RF and gradient waveforms for increasingly complex magnetic resonance imaging methods, we feel that this is a natural direction for the further development of spectroscopic NMR equipment in order to make it less expensive and available to areas where the high cost is presently prohibitive for the application of NMR. In order to make the method practically useful we suggest using an approach analogous to the currently existing “gradient shimming” where the gradient coils are used to create spatial maps of the B_0 homogeneity from which the correct values of the currents through the shim coils are calculated. With the shim pulses, the same gradient coils can be used for both the mapping and the correction of the B_0 inhomogeneity.

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A new method for obtaining high-resolution NMR spectra for samples in inhomogeneous magnetic fields is demonstrated. A combination of radiofrequency pulses and modulated magnetic field gradients are used to periodically rewind the phase dispersion originating from the main magnetic field inhomogeneity. The high-resolution spectrum can be acquired in a single transient. Non-linear corrections in three dimensions are possible with a homogeneous radiofrequency field and three orthogonal magnetic field gradients.
